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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER

ART UNIT	PAPER NUMBER
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DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/254,529

Applicant(s)

KINGSMAN ET AL.

Examiner

Sumesh Kaushal

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 May 2001.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10 and 12-23 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10 and 12-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s) _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other

DETAILED ACTION

The applicant's response filed on Paper No. 11, 05/18/01 has been fully considered. Claim 15 is amended and newly filed claims 19-23 are entered.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 U.S.C. §112

In view of amendment of claim 15 the rejection under 35 U.S.C. 112, first paragraph, is withdrawn.

Claim Rejections - 35 USC §103

Claims 1-10 and 12-23 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Cohli et al (Antisense Res. and Dev. 4:19-26, 1994), Naldini et al (Science 272:263-267, 1996.), Hope et al (PNAS, 87:7787-7791, 1990) and Lisiewicz (WO92/21750, 1992), for the same reasons of record as set forth in the official action mailed on 11/15/00.

The applicant argues that Cohli does not disclose or suggest a retroviral vector whereby the selected gene is contained within an intron and Choli et al either alone or in combination neither teach or suggest the presently claimed invention (response, page 3, para. 3). The applicant further argues that coding sequence for the reporter gene lies out side the RRE containing intron and the REV system is not used to manipulate the expression of therapeutic gene (response, page 4, para. 2). The applicant further argues that Hope does not disclose or suggest any HIV vector comprising splice donor sequence, RRE and a splice acceptor sequence (response, page 4, para. 3). Discussing, Liziewicz et al the applicant further argues that therapeutic gene and RRE of present invention is located within an intron and RRE is not located

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within the intron of a therapeutic gene (response, page 5, para. 2). The applicant concluded that the combination of references cited herein do not teach or suggest the present invention.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case, Cohli et al teaches retroviral vectors (MoMuLV) expressing HIV-1 packaging signal and REV response element (RRE) in sense or antisense orientation wherein the RRE sequence are expressed under the control of HSV-tk promoter fused to HIV TAR element, while the packaging signal sequence are expressed under the control of HSV-tk promoter. Cohli et al further teaches that both RRE and packaging signal sequences are expressed as part of 3' untranslated region of NEO gene (page 19, abstract, page 23, fig-1). However, Cohli et al does not teaches a retroviral vector, wherein the vector contains splice donor sequence, RRE and splice acceptor sequences, and the expression of the gene of interest is driven by internal promoter (CMV). Furthermore, Cohli et al does not teaches a retroviral vector wherein the gene of interest is located within an intron in a transcription unit of the provirus. However, these deficiencies are cured by the secondary references as cited below.

Naldini et al teaches a three plasmid retroviral expression system wherein the transfer vector comprising splice donor sequence, RRE and splice acceptor sequences (page 263, fig-1) Naldini et al further teaches the use of internal promotor CMV to drive the expression of a gene of interest (page 263, fig-1). Naldini further teaches the in-vitro transduction of host cells using the recombinant viral particles (page 264 table 1). Naldini clearly teaches that presence of RRE allows efficient transcription and cytoplasmic export of full length vector transcripts in the presence of HIV Tat and Rev regulatory proteins (page 263, col.2 para.1).

Hope et al teaches that HIV-1 transactivator Rev is a nuclear protein that regulates the expression of HIV transcripts by binding to the Rev response elements (RRE) present in the HIV transcripts. Hope et al further teaches a retroviral vector comprising splice donor sequence, RRE and splice acceptor sequences, wherein the gene of interest (CAT) is located within the splice donor and splice acceptor site (page 7787, abstract; page 7788, fig-1). Furthermore, the transcripts produced by the HIV vector harbor a single intron which contain CAT coding sequences (page 778, col.1. Para.1). Hope et al teaches the infection of MT4 cells with recombinant viral particles (page 21 col.2 para.2).

Liziewicz teaches a retroviral vector incorporating Rev/RRE system, wherein the RRE or functional equivalent thereof is located within the transcriptional unit of the foreign gene or within the transcriptional unit of the vector (page 6, line 21-32 page 9, line 1-4 and fig. 1-4). Liziewicz further teaches that the vector contain an internal promoters operably linked to the foreign gene and DNA sequence encoding the RRE (page 9, line 5-26). Therefore the invention as claimed clearly read upon the retroviral vector disclosed by Liziewicz wherein the gene of interest is located with in intron in the transcription unit of the provirus (see fig 1-4, page 9 line 1-26).

Thus it would have been obvious to one ordinary skill in the art at the time of filing to modify the retroviral vector as taught by Cohli et al with the insertion of splice donor sequence, RRE and splice acceptor sequences wherein the expression of the gene of interest is regulated by an internal promotor (CMV) as taught bu Naldini et al. It would have been further obvious to modify the teaching of Cohli and Naldni et al by inserting the gene of interest within the splice acceptor site as taught by Hope et al. It would have been further obvious to modify the retroviral vector as taught by Cohli, Hope and Naldni with the insertion RRE element into the intron of the foreign gene contained within the vector. In addition, in vitro transdcution of host cell using the vector as claimed is obvious in view of the cited references. One would have been motivated to do so because the insertion of a RRE into the intron of foreign gene and with in splice donor and splice acceptor sites provides the regulation of the expression of a foreign gene by RRE element. Therefore the invention as claimed is prima facie obvious in view of the prior art of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is (703) 305-6838. The examiner can normally be reached on Monday-Friday from 9:00 AM to 5:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Deborah Clark can be reached on (703) 305-4051. The fax-phone number for the organization where this application or proceeding is assigned as (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the patent analyst Tracey Johnson, whose telephone number is (703) 308-0377. If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 (<http://www.uspto.gov>) and A CLEAN COPY OF ALL PENDING CLAIMS IS REQUESTED to facilitate further examination.

SUMESH KAUSHAL
PATENT EXAMINER

Scott D. Pribe
SCOTT D. PRIEBE, PH.D.
PRIMARY EXAMINER